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DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
Office of the Director

Justification

Office of the Director

Authorizing Legislation: Section 301 of the Public Health Service Act, as amended. Reauthorizing legislation will be submitted.

Budget Authority:

FY 2003 Actual		FY 2004 Amended President's Budget		FY 2005 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
598	$285,894,000	598	$327,089,000	604	$359,645,000	6	$32,556,000

This document provides justification for the Fiscal Year 2005 activities of the Office of the Director (OD), including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2005 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)."

INTRODUCTION

The OD provides leadership, coordination, and guidance in the formulation of policy and procedures related to biomedical research and research training programs. To provide this direction, the OD centrally coordinates NIH's extramural and intramural research activities; science policy and related social, ethical, and legal issues; technology transfer and intellectual property protection policies; health information dissemination and education functions; legislative activities; and oversight of the agency's stewardship of public funds.

The OD encourages and fosters NIH research and research training efforts in the prevention and treatment of disease through program coordination offices that complement the efforts of the NIH Institutes and Centers (ICs). These offices focus on Acquired Immune Deficiency Syndrome (AIDS); women's health; disease prevention; science education; dietary supplements; rare diseases and disorders; and behavioral and social sciences research. While the OD provides the overall direction, coordination and oversight of these programs, the ICs manage the actual research operations. The OD is also responsible for coordinating trans-agency efforts for the NIH Roadmap. Initiatives under the NIH Roadmap are described at the end of this document.

The Office of AIDS Research

Introduction

The NIH Office of AIDS Research (OAR), coordinates the scientific, budgetary, legislative, and policy elements of the NIH AIDS research program and serves as the principal liaison with HHS, other federal agencies, and domestic and international governmental and non-governmental organizations on behalf of NIH AIDS-related research. The NIH represents the largest and most significant public investment in AIDS research in the world. Our response to the epidemic requires a unique and complex multi-institute, multi-disciplinary, global research program. Perhaps no other disease so thoroughly transcends every area of clinical medicine and basic scientific investigation, crossing the boundaries of the NIH Institutes and Centers. This diverse research portfolio demands an unprecedented level of scientific coordination and management of

research funds to identify the highest priority areas of scientific opportunity, enhance collaboration, minimize duplication, and ensure that precious research dollars are invested effectively and efficiently. This is recognized in the unique role given the OAR in its authorizing legislation, the NIH Revitalization Act of 1993. That law establishes OAR as a model for trans-NIH coordination, vesting it with primary responsibility for overseeing all NIH AIDS-related research, and thus allowing NIH to pursue a united research front against the global AIDS epidemic.

Comprehensive AIDS Research Plan and Budget: Each year, OAR oversees the Congressionally-mandated development of the comprehensive NIH AIDS-related research plan and budget, based on scientific consensus about the most compelling scientific priorities and opportunities that will lead to better therapies and prevention strategies for HIV disease. The planning process is inclusive and collaborative, involving the NIH institutes through a series of trans-NIH Coordinating Committees, as well as eminent non-government experts from academia, foundations, and industry, with the full participation of AIDS community representatives. Historically, the Plan has established the NIH AIDS research agenda in the following Scientific Areas of Emphasis: Natural History and Epidemiology; Etiology and Pathogenesis; Therapeutics; Vaccines; and Behavioral and Social Science. As the epidemic evolved, OAR recognized the need to bring additional focus to a number of cross-cutting areas. The Plan now also includes: Racial and Ethnic Minorities; Women and Girls; Microbicides; HIV Prevention Research; International Research; Training, Infrastructure, and Capacity Building; and Information Dissemination.

The Plan is a critical document, as it serves as the framework for developing the annual AIDS research budget for each Institute and Center; for determining the use of AIDS-designated dollars; and for tracking and monitoring those expenditures. The law provides that the OAR shall allocate all appropriated AIDS research funds to the Institutes. This process allows the OAR to ensure that NIH AIDS-related research funds will be provided to the most compelling scientific opportunities, rather than distributed simply by a formula.

Trans-NIH Coordination: During the course of the year, OAR identifies scientific areas that require focused attention and facilitates multi-institute activities to address those needs. OAR fosters these efforts by designating the bulk of its resources to jump-start program areas by providing funds and supplements to the Institutes and Centers; establishing working groups or committees; sponsoring workshops or conferences to highlight a particular research topic; and sponsoring reviews or evaluations of research program areas. For example, a number of years ago OAR identified microbicides research as an area needing additional attention. OAR established a Trans-NIH Microbicides Working Group, comprised of program staff of relevant institutes and offices; co-sponsored the first international conference on microbicides; spearheaded the development of an NIH Strategic Plan for Microbicides and a broader government-wide plan; and provided supplemental funds to the institutes to accelerate microbicide research. OAR also has placed high priority on research to address the disproportionate impact of the epidemic on racial and ethnic minority communities in the U.S. by directing increased resources toward: 1) new and innovative interventions that will have the greatest impact on these groups and 2) efforts to improve research infrastructure and training opportunities for minorities.

International AIDS Research: OAR coordinates, monitors and fosters plans for NIH involvement in international AIDS research and training activities. OAR established a new initiative and strategic plan for global research on HIV/AIDS aimed at significantly expanding our

our efforts to benefit resource- and infrastructure-poor nations. OAR has designated funds for the Institutes to expand clinical research internationally, including in the areas of microbicide development, identifying therapeutic approaches appropriate for international settings, vaccine research, and research capacity building.

Other OAR Activities: OAR supports Coordinating Committees for each research discipline of AIDS research. These committees allow OAR to stay abreast of the scientific programs across the NIH, to foster collaboration and coordination, and to develop the annual NIH plan and budget. OAR administers an emergency discretionary fund, and the Congress has provided a transfer authority that permits OAR to move up to a total of 3% of AIDS research funds between institutes. OAR supports the Intramural AIDS Targeted Antiviral Program and the NIH AIDS Research Loan Repayment Program. OAR also supports a number of initiatives to enhance dissemination of research findings to researchers, physicians, institutions, communities, constituency groups, and patients, particularly in minority communities.

The FY 2005 budget request for the OAR is $61.435 million. The OAR budget justification for NIH AIDS research appears under a separate tab in this Congressional Justification.

The Office of Research on Women's Health

Introduction

The Office of Research on Women's Health (ORWH) serves as the focal point for women's health research at NIH, with the authority and responsibility to act on behalf of the NIH Director to monitor and coordinate the activities of the NIH ICs regarding research on women's health. The Director of ORWH: (a) advises the NIH Director and staff on matters relating to research on women's health; (b) strengthens and enhances research related to diseases, disorders, and conditions that affect women; (c) ensures that research conducted and supported by NIH adequately addresses issues regarding women's health; (d) ensures that women are appropriately represented in biomedical and biobehavioral research studies supported by the NIH; (e) develops opportunities for and supports recruitment, retention, re-entry, and advancement of women in biomedical careers; and (f) supports research on women's health issues. The ORWH establishes a research agenda for women's health research, sets associated programmatic priorities, and also encourages, develops, and supports programs and opportunities for the recruitment, retention, advancement, and re-entry of women in biomedical careers. The ORWH collaborates closely with NIH ICs and the scientific and advocacy communities to continually update and implement the comprehensive NIH research agenda on women's health, and to provide funding and/or cofunding through the ICs for scientifically meritorious research and career development programs on women's health. In addition, the ORWH has established, through collaboration with the Office of Intramural Research (OIR), the Intramural Program on Research on Women's Health (IPRWH). The goal of the IPRWH is to serve as the focal point for all intramural women's health research, including sex and gender comparisons, within the Intramural Research Programs (IRP) at the NIH. The IPRWH consists of three subcommittees: 1) Women's Health Special Interest Group (WHSIG) - which hosts speakers for the intramural community; 2) Training – which is developing four intramural programs (clinical fellowship in women's health, shared postdoctoral fellow program, research career redirection program, and a research re-entry program); and 3) Outside Support/Grants to support cooperative, collaborative and interdisciplinary projects through grants. The ORWH Women's Health Seminar Series continues to be well received throughout the NIH and the neighboring scientific

received throughout the NIH and the neighboring scientific and lay communities.
The FY 2005 budget request for the ORWH is $41.577 million an increase of $.657 million above the FY 2004 level.

Science Advances

Specialized Centers of Research on Sex and Gender Factors Affecting Women's Health (SCORs): ORWH funds a program to foster interdisciplinary research on sex and gender factors in health. This program, which carries a five-year commitment, also receives cofunding by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute of Child Health and Human Development (NICHD), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the National Institute on Drug Abuse (NIDA), the National Institute of Mental Health (NIMH), the National Institute of Environmental Health Sciences (NIEHS), and the Food and Drug Administration (FDA). These Centers provide opportunities for interdisciplinary approaches to advancing studies on how sex and gender factors affect women's health by promoting interdisciplinary collaborations and develop a research agenda bridging basic and clinical research on sex/gender factors underlying a priority health issue.

The research scope of the SCORs stems from three sources: the Institute of Medicine (IOM) report, "Exploring the Biological Contributions to Health: Does Sex Matter?", "An Agenda for Research on Women's Health for the 21st Century," and recommendations from the NIH ICs. The funded Centers have elected to study areas such as pain, substance abuse, and urinary tract infection, among others. The research must bridge basic research to clinical interdisciplinary research and applications, to advance scientific discoveries from the laboratory into the clinical setting. Topical research themes of the SCOR Centers also include: Pharmacology of anti-epileptic and psychotropic medications during pregnancy and lactation; Role of sex and gender differences in substance abuse relapse; Genes, androgens and intrauterine environment in polycystic ovarian syndrome (PCOS); Sex and gender factors in the pathophysiology of irritable bowel syndrome (IBS) and interstitial cystitis (IC); Mechanisms underlying female urinary incontinence; Sex differences in pain sensitivity; Birth, muscle injury and pelvic floor dysfunction; Genetic and environmental origins of adverse pregnancy outcomes; Mechanisms by which drug transporters alter maternal and fetal drug exposure during pregnancy; and Molecular and epidemiologic basis of acute and recurrent urinary tract infections (UTI's) in women.

These interdisciplinary research programs have proved successful in mobilizing scientists of diverse disciplines to bring their scientific expertise to bear on examining how sex and gender factors contribute to health and disease. The SCOR program was recently evaluated by an External Advisory Committee which noted that Centers had already begun to demonstrate success in meeting their scientific objectives as well as to recognize and act on the need for broader collaborative efforts among their respective institutions. Significant progress has been demonstrated in each Center including development of experimental methodology, implementation and expansion of research, and recruitment of clinical participants. The SCOR program illustrates a highly effective mechanism to encourage and achieve interdisciplinary research and is already showcasing success in research on gender-specific differences in health and disease. Collaborations in research between Centers is already underway in several institutions.

Building Interdisciplinary Research Careers in Women's Health (BIRCWH): The ORWH initiated the BIRCWH program in FY1999 with cosponsorship from many NIH ICs and the Agency for Health Care Research and Quality (AHRQ). Twelve Centers were funded in FY2000 and an additional 12 in FY2002. This interdisciplinary career development program has proved very successful in ensuring a cadre of researchers transition smoothly from junior to senior status in areas of women's health research. To date, there are marked successes among the more than 100 scholars in the program who have advanced to a more senior faculty level supported by the large number of research grants these scholars have already been awarded. Scholars are performing interdisciplinary research in the areas of mental health, diabetes, cardiovascular disease, arthritis/musculoskeletal health, molecular biology/genetics, cancer, substance abuse, neurological disorders, and reproductive health.

Chronic Fatigue Syndrome: Chronic Fatigue Syndrome (CFS) is a debilitating and complex syndrome that may involve multiple bodily systems and is characterized by profound fatigue, which is not alleviated by bed rest, and can be exacerbated by physical or mental activity. Persons with CFS often function at substantially lower levels of activity from their pre-onset capacities. Neither a specific cause, diagnostic test, nor treatment has been identified for this illness. It is possible that multiple subcategories of conditions are subsumed under this rubric. Approximately one percent of the total US population is affected. Caucasian women suffer with this condition more frequently than do men or women from other ethnic groups; however, epidemiologic studies conducted on inner city populations suggest that these gaps may be narrowing. Important also is that approximately 80% of people identified in such studies have not been diagnosed or treated. In addition, there is a substantial pediatric population included in the whole.

The ORWH assumed responsibility for coordinating CFS research efforts through the Trans-NIH Working Group on Chronic Fatigue Syndrome Research (CFSWG) in FY2001. In FY2002, ORWH spearheaded the preparation of a new program announcement to stimulate and broaden the scope of CFS research (<<http://grants.nih.gov/grants/guide/pa-files/PA-02-034.html>>). In FY 2003, the first applications acknowledging this program announcement were received for scientific review and several have been funded. One, in particular, a five-year prospective study of CFS in adolescents reflects the call for multi- and interdisciplinary approaches to the causes, consequences and treatment of CFS over the lifespan and was jointly funded by ORWH and NICHD. The ORWH, through the CFSWG, held a scientific workshop on the interface between the brain and immune systems: Basic Mechanisms in Chronic Fatigue Syndrome: Neuro-Immune Mechanisms in June 2003. This initiative was designed to increase scientific knowledge about CFS and other similar multisystemic illnesses. Conclusions from this workshop suggest that CFS is one of several overlapping conditions that may share a common pathophysiology. Prominent among these diseases is a dysregulation in any one of several but interconnected body systems so that a perturbation in one affects the whole. Thus, these conditions cannot be studied in a linear model because they are disorders of homeostatic series. Overall, participants gained a better understanding of how the brain fits into the schema for understanding these conditions because it controls and mediates all interactions between the individual and his environment. Scientific advances make it possible to study CFS and similar

study CFS and similar conditions using this model but will prove difficult and expensive. The CFSWG is in the process of considering these recommendations and determining whether sufficient funding can be made available to issue an RFA based on these principles. and the possibility of issuing a new RFA based on these principles. ORWH continues to maintain a website for CFS and to work with other governmental and non-governmental agencies to foster CFS research programs.

Research Program: ORWH's research grant support has contributed to overall gains in knowledge about women's health. The areas covered by recent grants co-funded by ORWH include: evaluating sex (biological) and gender (societal) differences between men and women for many health conditions for which information on women may not have been previously available; healthy living and the prevention of chronic diseases; interdisciplinary approaches to multi-system diseases such as Chronic Fatigue Syndrome; mental health and addictive disorders; reproductive health; cancers in women; complementary and alternative medicine; and research on specific organ systems such as cardiovascular, kidney, and gastrointestinal.

One area in particular has to do with a greater understanding of the underlying mechanisms associated with autoimmune disorders such as systemic lupus erythematosus (lupus). Recent basic science and clinical grants are focusing on sex-based differences in anti-viral immunity in lupus, and the predictors of pregnancy outcome in lupus. Thrombosis and pregnancy loss are common features of lupus, particularly in the presence of antiphospholipid (aPL) antibodies. The in vivo mechanisms by which aPL antibodies lead to vascular events and specifically to recurrent fetal loss are largely unknown. Using the murine model of aPL has shown that in vivo complement activation is necessary for fetal loss caused by aPL antibodies. This research represents one of the first efforts to translate novel research observations on the potential role of complement activation in the pathogenesis of aPL antibody-mediated pregnancy loss to a clinically relevant human study.

Another recent advance focuses on vaccine development related to the transmission of Human Papillomavirus (HPV), which is a major cause of cervical cancer worldwide. Clinical trials co-funded by ORWH and the National Cancer Institute (NCI) are underway that will test whether vaccination with the HPV vaccine developed by the NCI will protect against the development of in situ and invasive cervical cancer. This research has the potential to result in a vaccine that would then prevent the development of HPV-induced cervical cancer and its precursors.

ORWH New Initiatives

Interdisciplinary Specialized Centers of Research (SCOR) on the Biology of Sex and Gender Differences (RFA): The ORWH, in conjunction with the NIH ICs and other DHHS agencies such as the AHRQ, would utilize budgetary resources to issue a second RFA in FY 2005. A new RFA would emphasize current research priorities not addressed in response to the first RFA. These efforts will provide sex/gender analyses of basic and clinical biological factors that contribute to the differences between men and women in health status and health outcomes. Special areas of research focus that may be addressed by such Centers include:

A. Interdisciplinary Approaches to Chronic Multisystemic Diseases with Multifactorial Etiology
B. Sex/Gender Differences in Response to Therapeutic Interventions

C. Care-giving and Health-related Quality of Life Issues
D. Kidney and Urologic Health
E. Neurobiology, including the examination of sex and endocrine differences in manifestations of brain health and of brain disorders
F. Complementary and Alternative Medicines and Dietary Supplements
G. Specific Organ Systems for which sex and gender studies are needed.

In addition, research priorities related to understudied areas of sex and gender factors in health and disease will be encouraged.

Building Interdisciplinary Research Careers in Women's Health (BIRCWH) RFA:

The ORWH will reissue the institutional career development award for a third cycle with collaborating ICs and other DHHS agencies for the "Building Interdisciplinary Research Careers in Women's Health (BIRCWH III) Career Development Programs." This mentored RFA supports research career development of junior faculty members, known as Interdisciplinary Women's Health Research (IWHR) Scholars, who have recently completed clinical training or postdoctoral fellowships, and who are commencing basic, translational, clinical and/or health services research relevant to women's health or sex and gender factors. There is great interest in the extramural community for continuation of existing BIRCWH centers as well as desire to establish new centers for interdisciplinary career development for junior faculty as interdisciplinary research scholars are currently a focus of great interest and the BIRCWH programs have provided an excellent model. The intent will be to allow existing programs to compete as well as to expand the number of centers based upon available resources. This solicitation, which has the potential to encourage underrepresented scientists into research careers to apply, will focus specifically on institutions that address populations that experience health disparities. Awards will seek to include areas of research not included in previous research program awards or that can enhance collaborative efforts in similar or related research at new sites. This initiative also promotes the performance of research and transfer of findings into clinical practice.

Current areas of scholar research include: mental health, diabetes, cardiovascular health, arthritis/musculoskeletal health, neurologic disorders, menopausal hormone therapy, sex/gender research/substance abuse, reproductive health, cancer research, molecular biology/genetics, health services/disparities, and trauma.

ORWH plans to continue funding these Centers through a recompetition RFA in FY 2006 and would begin efforts to issue a new BIRCWH announcement in FY2005 that would allow an additional emphasis on sex and gender factors to ensure a sufficient supply of women's health researchers for the future.

Awards from this RFA will provide clinical, health or life sciences, or public health departments, centers, and institutes an opportunity to build national capacity for junior investigators in women's health research, here defined as including research on sex and/or gender differences, as well as research on factors that contribute to disparities in health status or health outcomes for different populations of women. Projects may be basic, translational, clinical, or health services research, but must be within the biomedical and behavioral purview of NIH and/or the health services research purview of the AHRQ or additional DHHS entities that would consider cofunding this initiative.

Chronic Multisystemic Diseases: Today, chronic and complex conditions may require an integrative interdisciplinary approach that takes into account all facets of an individual's

individual's biologic, psycho-social make up in the context of and in interaction with the environment. In the past, these diseases have often been relegated to study in a linear model within a single scientific discipline. However, the ORWH now encourages interdisciplinary research approaches to such complex conditions through collaboration with multiple, appropriate NIH institutes. Whether it is because they seek medical care more frequently or because of their biological and psycho-social differences, more women than men are afflicted with these conditions that can include Chronic Fatigue Syndrome (CFS), Transmandibular Joint Disorder (TMJ), Irritable Bowel Syndrome (IBS), Fibromyalgia (FM), chronic pain, chronic inflammation, and chronic orthostatic intolerance and are often contributors to major mood disorders. It has become evident that these conditions are not only overlapping but may also share a common pathophysiology. In FY2004, ORWH served as the catalyst in the creation of an intramural special interest group composed of scientists and clinicians with expertise and interest in these chronic multisystemic conditions. Resources in the FY 2005 request would permit the creation of a pilot program within the NIH to test the principles of scientific integrative medicine, a discipline that combines molecular genetic with integrative physiologic approaches, that can be facilitated through this interest group. It is
anticipated that this approach can facilitate a more rapid understanding of these complex disorders and permit clinical translation that can assist patients in overcoming these disabilities.

Benign Uro-Gynecological Conditions: ORWH has had a long-standing commitment to fostering greater research in the area of benign uro-gynecological conditions such as uterine fibroids, pelvic floor disorders, urinary incontinence, and endometriosis. In recent years, there has been a special emphasis on fostering more uterine fibroids research because of the prevalence of this condition and the health disparities that exist in certain sub-populations of women.

In addition to supporting uterine fibroids research, ORWH will collaborate with a number of NIH institutes and centers to develop a state-of-the-art scientific conference that will bring together the leading intramural and extramural scientists to determine what are the next phases of research and other initiatives.

Prevention Research on Women and Girls: There is increasing evidence from research findings that many chronic health conditions have their origins in early life and young adulthood. Further, there is ample documentation of the extraordinary costs of unhealthy living, risky behaviors and non-adherence to screening and detection recommendations. Because women are such an integral point of our health care system and serve as decision-makers about health, ORWH plans to undertake several activities in FY 2005.

ORWH, working through its IC representatives and the DHHS partners' agencies, will coordinate a major conference on Prevention Research on Women and Girls. This conference will focus on current research and future areas of opportunity in such areas as the impact of diet, nutrition, exercise and weight patterns regarding chronic and multi-system diseases, and studies of behavioral, social and community factors on susceptibility to or protection from disease. The proceedings from this conference will provide the basis for possible future research initiatives focused on prevention of chronic

chronic diseases in women and girls.

Research Teams of the Future - Career Path Issues for Global Women in Health Sciences

At an October 2003 colloquium on career path issues facing women in the life sciences, including those in the developing world, ORWH, the Fogarty International Center (FIC) and the National Institute of Environmental Health Sciences as co-sponsors, heard from a community of scientists, administrators and science funding agencies about needs and opportunities in advancing career issues for women in the life sciences. FIC and ORWH will pursue this agenda in FY 2005 to support the development of data in developing countries on key features of career progression for women in the life sciences, to support workshops intended to develop skill sets for women scientists in the developing world to better enable them to take on leadership roles within health research and/or policy settings, and to develop and implement strategies to effectively utilize the Internet and other information technologies to network, to mentor and otherwise support women in the life sciences internationally.

The Office of Behavioral and Social Sciences Reserch

Introduction

The Office of Behavioral and Social Sciences Research (OBSSR) furthers the mission of NIH by emphasizing the role that behavioral and social factors and their interaction with biomedical variables play in health. The three main goals of the Office are to 1) enhance behavioral and social sciences research and training; 2) integrate a biobehavioral perspective across NIH; and 3) improved communication among health scientists and with the public. Specifically, the major responsibilities of the Office include the following:

- providing leadership and direction to increase the scope of and support for behavioral and social sciences research and training at the NIH;
- advising key NIH officials on matters relating to behavioral and social sciences research;
- serving as the principal spokesperson on the importance of behavioral and social sciences research in the acquisition, treatment, and prevention of disease and disability;
- stimulating research in the behavioral and social sciences and interdisciplinary research;
- providing leadership in disseminating finding from behavioral and social sciences research;
- and sponsoring seminars, workshops, and conferences at the NIH and at national and international scientific meetings on behavioral and social sciences research.

Since its establishment in 1995, the Office has made significant progress in fulfilling each of its mandates, including organizing 19 trans-NIH funding activities, sponsoring eight major conferences and cosponsoring multiple workshops and trans-NIH planning groups. The budget request for OBSSR in FY 2005 is $26.321 million.

Science Advances

Training for Conducting Behavioral Randomized Clinical Trials. The relevance of behavioral and social processes and interventions to health research has become increasingly clear over the past three decades. Research findings are now at the level where evaluation of interventions through Randomized Clinical Trials (RCTs) is becoming more and more necessary. However, behavioral RCTs present unique challenges (e.g., the identification and implementation a proper "placebo" or control group), and few behavioral scientists have training or experience in conducting RCTs. In consultation with experts, OBSSR developed and fully financed a 12-day-long Summer Training Institute for Randomized Clinical Trials Involving Behavioral Interventions, which it held in 2001, 2002, and 2003. Each year more than 400 scientists have expressed interest in the course, and more than 200 submitted applications for the 30 fellowships. The participants rated the training experience as "excellent." With the goal of creating a cadre of behavioral and biomedical scientists trained in evaluating behavioral interventions, OBSSR has awarded a competitive contract to Mt. Sinai Medical School and Columbia University to conduct
the Summer Training Institutes for five years and to expand the number of fellows to 35-40 per summer. In addition, OBSSR organized a well-received series of symposia to provide similar training to NIH staff in FY 2003.

Expanding the Initiative on Mind-Body Interactions and Health. The Public Health Service has documented that many of the leading causes of morbidity and mortality in the US are attributable to social, behavioral, and lifestyle factors (e.g., tobacco use, lack of exercise, poor diet, and alcohol abuse). Numerous studies have also documented that psychological stress is linked to a variety of health outcomes, and researchers and public health officials are becoming increasingly interested in understanding the nature of this relationship. Research has shown, for example, that psychological stress can contribute to increased heart disease and decreased immune system functioning. In FY 1999 the NIH issued a Request for Application (RFA) for Centers for Mind-Body Interactions and Health (OD-99-005) and subsequently awarded five P50 Center Grants (http://obssr.od.nih.gov/RFA_PAs/MindBody/mbpage.htm). In anticipation of the termination of these grants in FY 2004, OBSSR, in cooperation with NIH ICs, issued two RFAs for *Mind-Body and Health Research Infrastructure or Development Programs* and a third RFA for regular research grants (R01). The primary purposes of the RFAs are to provide resources to support and advance research that will improve the understanding of mind-body interactions and health, facilitate interdisciplinary collaboration among investigators conducting health-related mind-body research, and promote innovative approaches to mind-body and health research questions. An additional goal is to facilitate interaction among scientists in locations throughout the US in order to contribute to the integration and coordination of mind-body and health research. The RFAs will support approximately six center-like grants and four smaller developmental grants as well as about ten research grants commencing at the close of FY 2004.

Promoting Adherence to Medical Treatments. Lack of adherence to therapeutic regimens may result in poorer health for individuals as well as economic costs for their

health-care organizations and the broader society. The reasons for non-adherence are multifaceted and not fully understood. Health-care providers, organizational systems, and personal factors all play a role in adherence to therapeutic regimens. Thus, to understand and eventually improve adherence, conceptual frameworks and interventions need to take into account institutional, system, situational, interpersonal, and personal factors as well as the characteristics of the illness or condition and of the treatment regimen. In response to the public health significance of such issues as these, the NIH has issued a number of funding announcements in order to encourage fundamental and translational research. Among these is the FY 2000 RFA on *Testing Interventions to Improve Adherence to Pharmacological Treatments.* In order to continue to encourage and facilitate further research on adherence, compliance, and related issues, OBSSR created the **NIH Adherence Research Network**. Initially, consisting of NIH program staff from 16 Institutes, Centers, or Offices, it has been expanded to include over 200 non-NIH scientists. The Network provides electronic means for sharing information as well as sponsorship of periodic targeted meetings at the NIH and professional/scientific associations.

Allostatic Load and the Response to Trauma and Injury. Unintentional injury remains the lead cause of death for US citizens under the age of 40.[1] The physiological response to injury is exceedingly complicated. Two seemingly similar individuals with similar injuries often have widely different outcomes, possibly due, at least in part, to the fact that these individuals might actually arrive at the time of injury with very different life-experiences, having encountered a variety of factors which would impact their ability to respond to the injury. Allostatic load has been proposed as a measure of cumulative "wear and tear" on the body, *i.e.,* the price the body pays for having to adapt to various psychosocial challenges and adverse environments. It reflects interactions among genes, development, behavioral choices (e.g., diet, exercise, smoking), social interactions at the family, community and societal levels, and other life experience variables. In 2003, OBSSR and NIGMS sponsored a workshop to explore barriers to and opportunities for research on the topic of allostatic load and the response to traumatic injury. Workshop participants included neuroscientists, psychologists, immunologists, trauma surgeons, and physiologists. In response to the consensus recommendation that additional education of researchers in the relevant scientific disciplines is needed, OBSSR and NIGMS are planning to support symposia on this topic at 2004 annual meetings of the Shock Society and possibly the American Psychological Society. Following these development efforts, a PA to support research in this area could be issued in 2005.

Middle School Curriculum Supplement, "The Science of Healthy Behaviors." OBSSR, in collaboration with NINR and the NIH Office of Science Education, has recently contracted with Biological Sciences Curriculum Study to develop a curriculum supplement, entitled "The Science of Healthy Behaviors", aimed at middle school

[1] Anderson RN, Deaths: Leading Causes for 2000. National Center for Health Statistics (NCHS National Vital Statistics System, 2002.

students. This week-long set of modules will allow students to explore the scientific bases for the influence of behavioral and social factors on health and disease. The supplement will be developed, field-tested and prepared for widespread dissemination over a 4-year period that began in late FY 2003.

Exploring the Behavioral and Biological Pathways Between Education and Health. While the positive association between education and health has been well-documented, there is a paucity of scientific information on the biological mechanisms and the causal pathways which underpin this association. OBSSR, in collaboration with the NIA, NCI and NICHD released a RFA entitled *Pathways Linking Education to Health* in fiscal year 2003. The goal of this RFA was to increase the level and diversity of research directed at elucidating the causal pathways and mechanisms that may underlie the association between education and health. Better scientific understanding of the causal pathways between education and health could lead to additional and improved prevention and therapeutic intervention strategies for important health problems.
Applications in response to the RFA were reviewed by a Special Emphasis Panel convened by CSR on July 15, 2003. Thirteen research grants have been selected for funding in FY 2003 and 2004.

Making Behavioral Research More Relevant. The health care system is not making optimal use of the recent advantages in behavioral research. Research on altering harmful behaviors such as tobacco use, unhealthy dietary behaviors, inadequate physical exercise, and risky alcohol use or drug use demonstrates that it is possible to help patients initiate beneficial behavioral changes. Further research is needed to assist in making these behavioral therapies more practical, applicable to patients with more than one unhealthy behaviors, and successful in more diverse patient populations. In order to accomplish this goal, OBSSR is working in partnership with the Robert Wood Johnson Foundation (RWJF), the Agency for Healthcare Research and Quality (AHRQ), and the Centers for Disease Control and Prevention (CDC). In FYs 2002 and 2003 OBSSR and AHRQ funded an University based resource center to work with clinicians to incorporate the latest research findings into their practices and to conduct further research efforts to improve behavioral therapies. The resource center at the University of Indiana will work with the 17 primary care networks on a series of research projects to develop creative and practical strategies for promoting healthy behaviors among patients in their practices that can be easily adopted by other primary care practices.

Interactions of Work, Family, Health and Well-being. Family members often experience conflicts between the demands of work and family life. Foundation and federally funded research has begun to examine the role of family and work on the health and well-being of both families and employees. Scientific evaluation of these workplace programs will yield useful information about the effectiveness of these programs and about whether these potentially conflicting demands impact family and worker health and well-being. To address this issue, OBSSR jointly conducted a conference in FY 2003 with NICHD, CDC, and the Sloan Foundation. Previous research has examined the

has examined the relationships between work and health and between family and health, but not the interactions among all three. The goal of the conference was to foster communication between researchers working from these two perspectives, to identify the major gaps in knowledge, to discuss differences in research methods and theoretical approaches, and to foster cross-disciplinary research examining the interaction of paid work, family life, and health. Two subsequent conferences in FY 2004 will address methodological challenges of conducting this type of research and evaluation of existing or new intervention strategies.

Evaluating Complex Interventions. Randomized clinical trials have demonstrated the efficacy of a number of behavioral therapies and other types of therapies. Supplemental research strategies are needed to further evaluate how to apply the results of these randomized clinical trials to clinical practice, and to interventions that involve both clinical and community components. Some of this research will involve randomized trials in clinical settings or community settings but some may involve other research designs. This research has often been labeled as either effectiveness research or as research on defined populations. This research may involve systems level changes in health care systems. It may involve dissemination of information to clinicians, patients, and communities. The optimal research designs for this type of research need further exploration and the development of evaluation criteria for this type of research also need further development. In FY 2004, OBSSR working with NIH ICs and CDC is organizing a workshop on addressing the design and evaluation of this research.

Maintenance of Long Term Behavioral Change. Mounting evidence suggests the need for research that examines biopsychosocial processes and tests interventions designed to achieve long-term health behavior change. Research efforts funded by a recent OBSSR-coordinated RFA were successful in achieving behavioral change during and immediately following the intervention phase. However, other research indicates that relapse rates for addictive behaviors such as substance abuse and tobacco use are very high. For example, most individuals who stop smoking cigarettes relapse within six months. Adherence to exercise, diet and other health regimens is no better, despite the fact that initial success rates for various behavior change programs are very good. Thus long-term behavior change is as challenging, if not more so, than the initiation of behavior change. Past research efforts have typically focused on short term behavioral change. In FY 2004, OBSSR is implementing an initiative that encourages investigators to expand on the current theoretical base of change processes and intervention models, to expand our understanding of how change, once achieved, is maintained over the long term. Eleven grants have already been awarded under this initiative by the 10 participating NIH Institutes and Offices, and several other awards are anticipated.

OBSSR New Activities

Obesity Research Task Force. In the Spring of 2003, the NIH Director created the NIH Obesity Research Task Force as a new effort to facilitate progress in obesity research across the NIH, enhancing and synergizing the efforts of individual ICs. The Task Force consists of representatives from numerous NIH ICs and Offices, including OBSSR. The charge to the Task Force includes developing an NIH Strategic Plan for Obesity Research, monitoring implementation of the plan and reporting progress to the NIH Director and IC Directors, and serving as a point of contact between the NIH and relevant external agencies. OBSSR is participating in the development and funding of a number of new FY 2005 initiatives that emerged from the Task Force discussions. *The neurobehavioral basis of obesity* is an initiative to support research on the neural mechanisms underlying food intake and overeating, including the exploration of emotion, motivation, reward, sensation and perception, as well as social factors that influence ingestive behavior. *Prevention and treatment of pediatric obesity in primary care settings* will allow NIH to address the rising prevalence of childhood obesity by bolstering research on the development of prevention and treatment strategies in primary care settings. *The built environment and obesity* is focuses on elements of the built environment, such as aspects of community design that hinder physical activity, that may contribute to obesity. For example, large distances between homes, schools, and stores, and lack of sidewalks would necessitate motor vehicle use instead of walking. With this initiative, the NIH will seek to promote studies to identify and create instruments to measure the impact of healthful community environments on behavior and lifestyle choices. In addition, the OBSSR is supporting *Site-specific approaches for prevention or control of pediatric obesity*, a trans-NIH initiative developed by NIDDK, that will solicit grant applications for the prevention or treatment of pediatric obesity in various site-specific settings (e.g., family/home, day-care or pre-school, school, or other appropriate community venues).

Intramural, interdisciplinary training in the behavioral, social and biomedical sciences. It has become apparent that increasingly, scientific advances are being made at the interfaces of traditional disciplines, and that approaches to science are becoming more integrative. This requires a cooperative effort, typically in the form of investigators from diverse research backgrounds working collectively across traditional disciplinary boundaries to answer scientific questions and achieve specific endpoints. This also requires a workforce capable of crossing disciplinary boundaries and leading and participating in integrative and team approaches to complex health problems. OBSSR has begun development of a program to provide interdisciplinary training to postdoctoral fellows in NIH intramural laboratories. As currently envisioned, this program would provide a mechanism whereby an individual with a PhD in a behavioral or social science discipline, for example, might acquire interdisciplinary training that included biomedical research. Alternatively, someone trained in a more traditional biomedical field would receive postdoctoral training that included a behavioral or social science component. Each postdoctoral fellow would receive a 2-3 year training experience from two mentors, each from a different discipline. In addition to the benefits to be realized by the individual trainees, this program would also show NIH leading, by example, our Roadmap efforts to build Interdisciplinary Research Teams of the Future.

***Health Literacy*.** *Healthy People 2010* established a national health objective to improve health literacy by the decade's end. DHHS's initiative, *Healthy People 2010*, defines health literacy as the capacity to obtain, process, and understand basic health information and services needed to both make appropriate health decisions and use such information and services to enhance health. Health literacy pertains to individuals, communities and systems. As the sharing of relevant health information and the active participation in health care and health promotion efforts are dependent on health literacy, strengthening health literacy is a means to increase quality and years of healthy life and to eliminate health disparities. While many diseases and conditions can be prevented or controlled, too often people with the greatest health burdens have few fact-finding skills and the least access to health information. Moreover, health care providers may not be able to communicate effectively with these individuals. These situations hamper the effectiveness of health professionals' efforts to prevent, treat, and diagnose medical conditions. OBSSR and several ICs are working on a PA for research to increase the scientific understanding of the nature of the health literacy problem and its relationship to disparities in health outcomes and health communications problems and to test interventions to overcome the adverse consequences of low health literacy.

Workshop on "Difficult to Diagnose" Conditions. Physicians and dentists are often faced with a set of symptoms that do not clearly fit any one condition. The bio- or behavioral markers important in a distinct diagnosis of one of these conditions seem to be missing. As a result, the patient may be passed from one specialist to another, with no improvement in symptoms. The patient may ultimately be told that they are 'neurotic' (i.e., that the symptoms are not real and are the fault of the patient) rather than that the physician or dentist simply does not know what is wrong. Or the patient may be treated for something that is not the cause of the problem; as when, for example, patients with temporomandibular joint and muscle disorders (TMJ) receive implanted jaw joints when something far less invasive is warranted. Not only TMJ sufferers but also those with several other conditions report having these negative experiences when seeking treatment. Some of these other 'difficult to diagnose' conditions include Sjogren's (dry mouth) disease, trigeminal neuralgia, seasonal affective disorder, irritable bowel syndrome, fibromyalgia, multiple chemical sensitivity, myofascial pain syndrome; chronic fatigue syndrome, and sleep disorders such as restless leg syndrome. In response to 2003 Senate report language asking the NIH Director to develop a coordinated research agenda in this area, OBSSR will work with NIDCR and other NIH ICs and Offices that support relevant research, as well as patient advocates and professional organizations, to convene a set of experts to develop a research agenda addressing this topic. The proceedings will be used to guide the NIH and the scientific community in laying out short- and long-term research objectives for the area of TMJ and other sets of complex conditions difficult for physicians and dentists to diagnose.

Social Work Research. Social workers focus on the creation of effective health and mental health prevention and treatment interventions in order for individuals to become more productive members of society. Social workers provide front line prevention and

treatment services in the areas of aging, teen pregnancy, child abuse, and substance abuse, particularly in underserved communities. Consequently, social workers are in a unique position to provide valuable research information on these complex social concerns, taking into account a wide range of social, medical, economic and community influences from an interdisciplinary, family-centered, and community-based approach. Faculty members and other researchers in the social work field widely agree that, although social work research and research development efforts have enjoyed an increasingly wide base of support across NIH, research initiatives are needed in areas that reflect the social work profession's uniqueness in dealing with public health issues and concerns. Hence, to provide the impetus and resources to fully incorporate social work's unique concepts and perspectives (e.g., person-in-environment across levels, client-centeredness, etc.) into the NIH research portfolio and to build the scientific base to be used by allied health professionals, OBSSR, NIDA, NIMH, NIAAA, NCI and other ICs are developing a new Program Announcement entitled *Developmental Research on Social Work Practice and Concepts in Health*.

The Office of Dietary Supplements

Introduction

The Office of Dietary Supplements (ODS) was established in 1995 under the Dietary Supplement Health and Education Act (DSHEA). The mission of ODS is: *to strengthen knowledge and understanding of dietary supplements by evaluating scientific information, stimulating and supporting research, disseminating research results, and educating the public to foster an enhanced quality of life and health for the U.S. population*. To achieve this mission, ODS in 1998 released its first Strategic Plan. This plan identified five scientific and communications goals. Substantial increases in ODS budget over the last four years, has made it possible to make significant progress toward meeting these five strategic goals and to develop new areas of research and education. It has also triggered the need for ODS to update its strategic plan in order to respond to the growing science and communication needs for dietary supplements. The updated plan is nearing completion and will be publicly available early in 2004 on the ODS website http://ods.od.nih.gov. To meet the program goals for FY 2005, the budget request for ODS is $26.218 million.

Science Advances

A. Dietary Supplement Analytical Methods and Reference Materials Program

Background: Senate report language accompanying the FY 2002 appropriation (and reiterated in the Senate report for FY 2003) called on ODS to establish a program to develop, validate, and disseminate analytical methods and reference materials, primarily but not exclusively for botanical supplement ingredients.

Advance: ODS created a new program to meet this challenge; the program has already begun to coordinate these activities among government agencies, non-governmental organizations, academia, and the private sector. These include the development and validation of analytical methods through AOAC International; the development of standard reference materials by National Institute of Standards and Technology; and partnering with the United States Pharmacopeia (USP) for production of USP reference materials for its dietary supplement monographs.

Saldanha LG, Betz JM, and Coates PM. Challenges in developing validated analytical methods and reference materials for dietary supplements: A summary of comments made at three meetings that contributed to the development of the National Institutes of Health?s Analytical Methods and Reference Materials Program. Journal of AOAC INTERNATIONAL, 2003 (in press).

B. Evidence-Based Reviews of Dietary Supplement Benefits and Safety

Background: In 2001, Senate and House Report language, encouraged the Office to examine the efficacy and safety of dietary supplements and to enhance clinical research on the safety and efficacy of ephedra-containing products. In 2002, Senate Report language accompanying budget appropriations for NIH called for the systematic review of literature related to the health benefits of omega-3 fatty acids, particularly with respect to heart disease. These recommendations resulted in the creation of an Evidence-Based Review Program within ODS. This program, developed in collaboration with the Agency for Healthcare Research and Quality (AHRQ) and its

Evidence-Based Practice Center (EPC) network, will systematically build the knowledge base on the benefits and safety of dietary supplements and, encourage research to fill gaps in the knowledge base.

Advance 1: The ephedra report: Released in FY 2003, the report concluded that ephedrine and ephedra were effective in promoting modest short-term weight loss (0.9 kg/month more than placebo) in small clinical trials of up to 4 months duration. There were no data regarding long-term weight loss. Evidence to support use of ephedra for athletic performance enhancement was of very poor quality. Ephedra or ephedrine (with caffeine) was associated with increased risk of psychiatric, autonomic, and gastrointestinal symptoms, and heart palpitations. Serious adverse events were also carefully evaluated as part of the report. The report provided detailed information about the state of the science for this ingredient. On December 30, 2003 the FDA issued a proposed rule to prohibit sales of dietary supplements containing ephedra. In developing future research activities on dietary supplements containing ephedra, the NIH will take the FDA’s proposed rule into consideration.

Shekelle PG, Hardy ML, Morton SC, Maglione M, Mojica WA, Suttorp MJ, Rhodes SL, Jungvig L, and Gagné J: Efficacy and safety of ephedra and ephedrine for weight loss and athletic performance: A meta-analysis. JAMA 289:1537-1545, 2003.

Advance 2: The omega-3 fatty acids reports: Senate Report language accompanying the FY 2002 budget appropriation for NIH called for the systematic review of literature related to the health benefits of omega-3 fatty acids, particularly with respect to heart disease. ODS has worked closely with the National Heart, Lung, and Blood Institute (NHLBI), as well as with other Institutes and Centers, to develop the task order for this review. Three EPCs (RAND-Southern California, University of Ottawa, and New England Medical Center) are collaborating to produce a series of reports on the effects of omega-3 fatty acids on a number of body systems/conditions including cardiovascular disease, infant growth and development, and mental disorders. As the completed reports become available over the next two years, ODS will work with NIH Institutes and Centers to develop appropriate research agendas.

C. Dietary Supplement Research Centers Initiative

Background: Initiated in FY 1999, this project is a joint effort of 3 NIH units: ODS, National Center for Complementary and Alternative Medicine, and National Institute for Environmental Health Sciences. There are currently six interdisciplinary Centers in the program. The National Institute of General Medical Sciences and Office of Research on Women?s Health have provided additional funding. All of these Research Centers, currently focused on botanical dietary supplements, were funded for an initial period of 5 years. The long-term goal of this program is to meet emerging priorities in dietary supplement research where an interdisciplinary approach is needed. The program underwent evaluation by external scientific reviewers in FY 2003 as a prelude to releasing a Request for Applications (RFA) for re-competition of the program in FY 2004. Funding for this initiative would begin in FY 2005.

D. Investigator-initiated Research

Background: ODS continues to support investigator-initiated research in partnership with other Institutes and Centers at NIH. In FY 2003, ODS expanded its portfolio of co-funded grants; ODS now collaborates with 14 Institutes and Centers (ICs) in funding 72 grants. Grant topics include basic studies of metabolism of dietary supplement ingredients, methods for botanical supplement analysis, in vitro and in vivo pre-clinical studies, and clinical trials of dietary supplements.

E. Training and Career Development

ODS is committed to expanding the career opportunities for investigators in dietary supplement research in collaboration with NIH ICs. Strategies include: travel support for young investigators to attend and present data at scientific meetings in the field of dietary supplements; co-funding of Fellowship and Career Development awards to young investigators; and funding the research career development of selected NIH intramural fellows.

F. Proceedings of Conferences

Background: ODS organizes a number of public conferences each year to further the understanding on the use of dietary supplements across the lifespan or on the role of dietary supplements in disease conditions. The 2002 *Dietary Supplement Use in Women of Reproductive Age* and 2003 *Dietary Supplement Use in the Elderly* were organized with the National Institute of Child Health and Human Development, and the National Institute on Aging. The *Diet, DNA Methylation Processes, and Health*, organized by the National Cancer Institute, ODS, and others led to the release of two research initiatives, a Program Announcement and an RFA, jointly sponsored by NCI and ODS in FY 2002.

Dietary Supplement Use in Women: Current Status and Future Directions. Proceedings published in the Journal of Nutrition, volume 133, ages 1957S-2013S, June 2003.

Ross SA and Poirier L: Proceedings of the HHS workshop: Diet, DNA Methylation Processes and Health. Journal of Nutrition 132: 2329-2332, 2002.

NIH Roadmap

Research Teams of the Future: ODS has been successful in collaborating with Institutes and Centers across NIH, other sister agencies, and for-profit and not-for-profit groups to achieve its goals. The *Dietary Supplement Analytical Methods and Reference Materials Program* and the *Evidence-Based Review Program* are examples of such collaborative efforts. ODS will continue to use this model to execute its revised strategic plan. Through high-level science-driven partnership meetings, it will identify scientific gaps in the knowledge base on dietary supplements, and stimulate novel areas of research to fill these gaps. An example of an initiative is the bioactive food components project. Discovery of the role these components play in promoting health and preventing chronic disease has resulted in widespread consumer use. Furthermore, epidemiological, pre-clinical, and clinical studies provide evidence that numerous food components are capable of improving health and well-being. ODS will partner with other public and private organization to investigate the practicability of developing new approaches for evaluating the health effects of these components.

Information and Education Goals

Searchable Databases: Updated quarterly, *International Bibliographic Information on Dietary Supplements* (IBIDS) database contains nearly 700,000 citations of published papers on dietary supplements. In FY 2001, ODS expanded the service to include the ability to search consumer-oriented literature contained in IBIDS, and is considering creating a clinical version of this database. Launched in FY 2002, *Computer Access to Research on Dietary Supplements* (CARDS) contains detailed information about research studies on dietary supplements funded by the federal government.

Fact Sheets: Ingredient specific, these facts sheets provide comprehensive information on individual vitamins, minerals, botanicals, and other components classified as dietary

supplements under DSHEA. Currently there are over 25 facts sheets that are available on the ODS Web site. These are regularly reviewed for timeliness and accuracy.

Annual Bibliography of Significant Advances in Dietary Supplement Research: Launched in 2000, this yearly publication provides a snapshot of original research that appeared in the scientific literature for the previous year. The 2002 issue highlighted 25 papers (selected from over 350 nominations) that appeared in 34 peer-reviewed scientific publications.

Presentations at Professional and Trade Meetings: ODS has made presentations about NIH funding strategies, ODS programs, and current issues in dietary supplement use to a wide variety of US and international audiences. These include professional academic society audiences, industry-sponsored meetings, and meetings sponsored by other non-governmental organizations. These efforts provide up-to-date information about research activities and opportunities for academic and industry-based investigators to compete for NIH funds in dietary supplement research.

ODS New Initiatives

Evidence-based Reviews of Dietary Supplement Efficacy and Safety: In collaboration with the NIH Office of Medical Applications of Research (OMAR) , ODS is planning a State-of-the-Science Conference on the Role of Multivitamins/Multiminerals in the Prevention of Chronic Disease. An evidence report will be prepared for this Conference, in consultation with many IH ICs. The Conference will be held in FY 2005. ODS is currently evaluating a variety of topics for additional evidence-based reviews; these include: 1) the role of vitamin and mineral supplements in chronic disease prevention; and 2) health effects of bioactive food components. Topics will be prioritized based on their potential as feasible research agendas, and several of them will be initiated in FY 2004.

Support for National Surveys of Dietary Supplement Use: ODS continues to support the National Health and Nutrition Examination Survey, conducted by the National Center for Health Statistics at the Centers for Disease Control and Prevention, for those aspects of the survey concentrating on dietary supplement use in the US population. This work will inform future research about dietary supplement use in important target populations, such as children, women, and the elderly. Funding from ODS is used to create and populate a database of dietary supplements to assist with the survey, as well as to support the measurement of blood levels of key metabolites associated with dietary supplement use. In addition, ODS is funding the creation of an analytically-substantiated database of dietary supplements, similar to the food composition database created and managed by the United States Department of Agriculture (USDA). The impetus for these efforts came from a workshop co-sponsored workshop with the Agricultural Research Service of USDA in 2002.

Madans JH, Sondik EJ, and Johnson CL: Future directions for What We Eat in America-

America-NHANES: The integrated CSFII-NHANES. Foreword. Journal of Nutrition 133: 575S, 2003.

Expansion of Efforts to Partner with Industry to Advance Research Goals: ODS is committed to developing opportunities with the private sector to enhance research efforts in the
area of dietary supplements. ODS continues to co-fund Small Business Innovation Research -grants in collaboration with other NIH ICs. ODS is regularly attends meetings of industry groups to provide information about NIH programs that may be of interest to them.

Other Areas of Interest

International Activities: Micronutrient deficiencies remain a problem in many parts of the world. The ODS partners with other NIH ICs, such as the Fogarty International Center (FIC), as well as other organizations within and outside the federal government, to improve the quality of research needed to implement effective micronutrient assistance programs in diverse settings around the world. ODS co-sponsors the NIH effort on Brain Disorders in the Developing World: Research Across the Lifespan. ODS will sponsor a networking session on dietary supplement assessment and use at the International Congress of Dietetics in FY 2004.

The Office of Rare Diseases

Introduction

The Office of Rare Diseases (ORD) supports activities that stimulate, coordinate, and support research on rare diseases and conditions. A rare or orphan disease is defined as a disease, illness,

syndrome, or condition affecting fewer than 200,000 Americans.[2] Although the prevalence of each disease may be quite small, more than 25 million Americans are estimated to suffer from the more than 6,000 known rare diseases. [3] [4]

The budget request for the ORD is $15.787 million, an increase of $.253 million above the FY 2004 level.

Science Advances

ORD together with the NIH Institutes and Centers supports seven Rare Diseases Clinical Research Centers and one Data and Technology Resources Coordinating Center, all of which together form the new *Rare Diseases Clinical Research Network*. The network consists of a consortium of investigators, institutions, and patient support organizations. In addition to the

[2] The definition of a rare disease is anchored in the Orphan Drug Act of 1983
[3] The Rare Diseases Act of 2002, P.L. 107-280: Findings (a)(2)
[4] The Rare Diseases Act of 2002, P.L. 107-280: Findings (a)(2)

increased focus on the particular rare diseases group, the benefit of each center will include a better integration of multisite, multidisciplinary research activities. Also, the distribution of research locations across the U.S. will make investigational treatments more accessible to patients with rare diseases. The goal for the network is the systematic collection of clinical information to develop markers and new approaches to diagnosis, treatment, and prevention of rare diseases, and to provide training of new clinical research investigators in the following rare diseases:

- Urea cycle disorders, such as ornithine transcarbamylase (OTC) deficiency, argininosuccinic synthetase deficiency (Citrullinemia), and N-acetylglutamate synthetase (NAGS) deficiency, and other disorders.
- Inborn errors of metabolism, including Rett syndrome, Angelman syndrome (AS), and Prader-Willi syndrome (PWS).
- Vasculitites including Wegener's granulomatosis, Takayasu arteritis and Churg-Strauss syndrome.
- Bone marrow failure including aplastic anemia (AA) and other idiopathic bone marrow failures leading to anemia, leukopenia, or thrombocytopenia.
- Rare genetic defects in steroidogenesis leading to congenital adrenal hyperplasia.
- Rare lung diseases including lymphangioleiomyomatosis (LAM), alpha-1 antitrypsin deficiency (AATD), pulmonary alveolar proteinosis (PAP), and hereditary idiopathic pulmonary fibrosis (hiPF).
- Nervous system channelopathies including periodic paralysis, nondystrophic myotonic disorders, and episodic ataxia.

In addition, the ORD cosponsored a Program Announcement with the National Heart, Lung, and Blood Institute for pilot studies, demonstration projects, and/or exploratory research studies in rare diseases and a Request for Applications with the National Human Genome Research Institute (NHGRI) for research training grants in genomics and proteomics.

The ORD continues to support a number of activities to stimulate, coordinate, and support research on rare diseases and conditions including co-funding with the National Human Genome Research Institute of the *Genetic and Rare Diseases Information Center*. The information center provides comprehensive, easily understandable, and valid information to patients and their families, health professionals, researchers, and to the public. ORD will support making the information center more accessible to minority and under-served populations.

The *Rare Diseases Intramural Research Program* is a collaboration between the ORD and the National Human Genome Research Institute as well as the NIH Warren Grant Magnuson Clinical Center, the clinical research facility at the NIH. The program includes an NIH focus to provide expert consultation from researchers for patients with rare diseases where a diagnosis has been elusive, followed by entry into clinical studies of treatments for rare diseases. This program will also elicit new research on diagnostic approaches and technology.

In addition, the ORD intramural research program supports research training for biochemical geneticists who focus on rare diseases, and five Bench-to-Bedside grants. The Bench-to-Bedside

grants encourage intramural clinical, translational, and basic scientists at the NIH to enter into basic science-clinical collaboration with colleagues in other NIH laboratories or clinics with a focus on research directly related to rare diseases.

Also, in FY 2003, ORD co-funded 61 national and international scientific conferences in collaboration with NIH Institutes and Centers with an emphasis on scientific opportunities or where little or no research exists on a particular rare disease or disease group. Examples of the scientific conferences in FY 2003 include: Amyotrophic lateral sclerosis, ataxia-telangiectasia, Batten disease, cystic fibrosis, rare digestive diseases, Duchenne muscular dystrophy, Hutchinson Gilford progeria, neurofibromatosis, sickle cell disease, and spina bifida.

In FY's 2003 and 2004, ORD supported a series of regional workshops to discuss with patient support groups across the nation all aspects of research and research opportunities in NIH's extramural and intramural research programs. These workshops will enable each national organization to strive toward full research access and partnering in the research endeavor.

ORD New Initiatives

Possible new initiatives include a rare diseases tissue bank and registry, expanded access to charitable patient travel to and lodging near research and treatment sites, and a feasibility study of a database of rare diseases patient support organizations to improve access to and participation in clinical research studies.

Science Education Activities

Introduction

The Office of Science Policy (OSP), through its Office of Science Education (OSE), coordinates science education activities at the NIH and develops model science education programs. OSE works to advance the NIH mission by: creating programs to improve science education in schools; creating programs to advance public understanding of medical science, research and careers; promoting NIH educational resources and programs; and advising NIH leadership about science education issues. OSE has a special interest in programs that benefit underserved communities, women, and minorities.

Current Activities & Initiatives

The OSE's programs target different sectors of the public: school systems– including teachers, school administrators, and students; and the general public. Certain programs serve overlapping target audiences.

The OSE's most important activity is the development and distribution of the NIH Curriculum Supplements and related professional development activities. These National

Science Education Standards-based K-12 supplements are free, ready-to-use, interactive teaching units that result from the unique partnering of NIH scientists, teachers, and expert curriculum developers. They incorporate the best of both science and education communities, and are intended to introduce new scientific concepts and supplement classroom materials that are out-dated.

Over 109,000 NIH curriculum supplements have been distributed to science teachers, college professors and home schoolers in all 50 states, the District of Columbia, Puerto Rico, U.S. Pacific Island territories and Department of Defense schools overseas.

The office continues to develop, field test, refine, and disseminate, new supplements each year. In collaboration with different NIH IC's, and the highly respected curriculum developer Biological Sciences Curriculum Study, OSE has 15 different curriculum supplements that are in various stages of development. By FY 2005, the office expects to distribute 6 high school units, 8 middle school units, and 1 elementary school unit. Hard copies of these materials will continue to be distributed to teachers, school administrators, and home-schoolers. In addition, Web versions of the first twelve supplements will be available and meet Section 508 accessibility standards. During FY 2005, one new middle school unit entitled *The Science of Healthy Behaviors*, will undergo national field-tests. Following a promising pilot study in New York City, OSE is collaborating on a larger evaluation with the National Science Foundation. Results from this evaluation will become available in FY 2005 and be used to refine the development of future supplements.

To enhance the effectiveness of the NIH Curriculum Supplements nationwide, OSE implements professional development programs for teachers. The office will continue to pursue partnerships with NIH-sponsored research centers, universities, professional societies, and science education organizations to maximize the number of teachers trained to use the NIH Curriculum Supplements.

In FY 2005, the OSE plans to begin using videocasting and Web technologies to enhance its professional development program for the NIH Curriculum Supplements. These technologies will allow OSE to “take the workshops to the teachers.” Teachers in under-served or remote areas are less likely to have funds available to travel to workshops. By implementing an online approach, we hope to reach a much larger audience than is possible with the current face-to-face workshops.

The OSE Web site (http://science.education.nih.gov) is a major means of informing science teachers nationally about NIH publications. In the past three years, traffic on the site has increased nearly five-fold, from about 6,000 to 30,000 users per month. The OSE Web site includes a unique career exploration section, *LifeWorks* (http://science.education.nih.gov/LifeWorks), for middle and high school students, their parents, teachers, and career guidance counselors. Launched in FY 2003, *LifeWorks*, provides in-depth career information on over 100 health and medical science-related careers. Users can search the site based on their abilities, personal interests, and the skills they want to acquire. Career-specific information includes educational requirements,

requirements, recommended high school courses, salary projections, job outlook, training and certification requirements, related careers, and references for further information. Interviews with NIH scientists and other individuals are currently being added to the site to serve as *real* career examples. Future enhancements include short video segments of "real people" in their working environment. In FY 2005 OSE will work to integrate the *LifeWorks* Web site with its speakers bureau. The *NIH Speakers Bureau* is comprised of research scientists, clinicians, and other NIH professionals who speak on a variety of health, medical and science research topics, and related careers to local schools and other community groups.

The Office of Science Education Exhibit Booth (http://science.education.nih.gov/exhibits) provides a forum for the 27 institutes and centers (ICs) that comprise the NIH to showcase and disseminate their free, and innovative science education resources to K-16 teachers and school administrators throughout the U.S. It is displayed at many national and regional conferences such as the National Science Teachers Association and the National Association of Biology Teachers.

Visitors to the booth can obtain free NIH resources for their classrooms and learn about the NIH and it's mission. Each year OSE is able to reach out to well over 10,000 science teachers through its participation at such conferences.

In partnership with the Office of Research on Women's Health (ORWH), the OSE developed two programs encouraging middle-school girls to consider careers in science. The first, *Women are Scientists Video and Poster Series*, consists of informative video and poster sets that depict successful women scientists as inspirational role models. Four sets are currently available, and a fifth, featuring women in dentistry will be developed. The second program is the *Careers in Science: Women in Research*. This is a series of posters with a companion Web site that emphasizes the different career options available within medical research, all of which are open to women. Three different posters are currently available. In both programs, the racial and ethnic backgrounds of the women depicted help to make the posters relevant to a large number of girls, in particular, those from populations currently under-represented in scientific and medical careers.

The OSE sponsors two popular education programs for the public. The *NIH Mini-Med School* (http://science.education.nih.gov/nihmms) is a 9-week program held in the spring that provides the public with an opportunity to experience what it's like to be a medical student. Students learn about current science and health topics from NIH's leading scientists in a relaxed environment. OSE has also worked with more than 60 other institutions to help them start their own local Mini-Med School programs. OSE maintains a Web site that lists these programs (http://science.education.nih.gov/mms). Another public education program, *Science in the Cinema*, is a free film and discussion series held in the summer for 6 consecutive weeks. Each week a film with a medical science theme is screened. Immediately following, an expert in the film's subject area leads the audience discussion about the science depicted in the film. Average attendance at this event has increased from 150 people per evening in 1994 to more than 750 people per evening in

evening in 2003.

Other Areas of Interest

In FY 2002, the OSE established the Diversity Work Group (DWG) – a team dedicated to increasing the participation of minority and under-served populations in all OSE programs. As a result of a DWG recommendation, the OSE will collaborate with the National Center for Minority Health and Health Disparities in FY 2005 to bring OSE programs to underserved communities. The budget request for OSE in FY 2005 is $3.899 million.

Loan Repayment and Scholarship Programs

Science Advances

In FY 2003, through the loan repayment and scholarship programs authorized under the NIH Revitalization Act of 1993, the NIH Clinical Research Loan Repayment Program for Individuals from Disadvantaged Backgrounds (CR-LRP) awarded a total of three (3) two-year contracts and ten (10) one-year renewal contracts at a cost of $.638 million. The awardees agreed to conduct clinical research as NIH employees during their contract period, while the NIH agreed to provide up to $35,000 repayment per year toward their educational debt. In addition to educational loan repayments, the CR-LRP provides Federal tax reimbursements at the rate of 39% of loan repayments made, as well as additional State and local taxes, as compensation for the increased tax burdens resulting from the receipt of loan repayments. For FY 2004, the CR-LRP plans to award contracts to five (5) individuals entering into initial two-year contracts, and ten (10) contracts to individuals entering into one-year renewal contracts at a cost of $.688 million.

In FY 2003 the NIH awarded $4.596 million to fifty-three (53) individuals under the Loan Repayment Program for Research Generally (GR-LRP). Awards were made to fund forty-two (42) initial three-year contracts and eleven (11) one-year renewal contracts to participants who are physicians or scientists engaged in either basic or clinical research activities at the NIH. This program is intended to recruit and retain health professionals to non-trainee NIH intramural positions; thus, such individuals will generally be considered for permanent and/or tenure-track positions. GR-LRP participants agree to a minimum service contract period of three years. In addition to educational loan repayments of up to $35,000 per year, the GR-LRP provides Federal tax reimbursements at the rate of 39% of loan repayments made, as well as additional State and local taxes, as compensation for the increased tax burdens resulting from the receipt of loan repayments. For FY 2004, the GR-LRP plans to award contracts to forty-four (44) individuals entering into initial three-year contracts, and twelve (12) contracts to individuals

entering into one-year renewal contracts at a cost of $4.346 million.

The NIH continued to support the Undergraduate Scholarship Program for Individuals from Disadvantaged Backgrounds (UGSP). In FY 2003, scholarship awards and funding for service pay-back were provided in the amount of $.793 million to fifteen (15) undergraduate students and sixteen (16) post baccalaureate students who agreed to pursue academic programs appropriate to support positions required by NIH's intramural research and training programs. In satisfaction of statutorily mandated service requirements, scholars agreed to employment at the NIH for one year for each year of scholarship support after graduation, with deferment of the service requirement possible for those who pursue appropriate graduate and medical school training, in addition to ten weeks during the academic year. For FY 2004, the UGSP plans to award scholarships and provide funding for summer internship service pay-back for twenty-one (21) individuals and provide funding for fourteen (14) individuals performing one-year service pay-back at a cost of $.943 million.

Future Research Directions

In FY 2005, the budget request is $7.250 million. The funding will be used for fifteen (15) awards under the Clinical Research Loan Repayment Program for Individuals from Disadvantaged Backgrounds, twenty-one (21) awards for the Undergraduate Scholarship Program for Individuals from Disadvantaged Backgrounds, and sixty-one (61) awards under the Loan Repayment Program for Research Generally.

AIDS Research Loan Repayment Program

Introduction

In FY 2003 the NIH awarded $.483 million to ten (10) individuals under the AIDS Research Loan Repayment Program (AIDS-LRP). Awards were made to ten (10) health professionals, representing four (4) recipients who entered into one-year renewal contracts and six (6) researchers who entered into initial two-year contracts. The awardees agreed to conduct AIDS research as NIH employees, while the NIH agreed to provide up to $35,000 repayment toward their educational debt. In addition to educational loan repayments, the AIDS-LRP provides Federal tax reimbursements at the rate of 39% of loan repayments made, as well as additional State and local taxes, as compensation for the increased tax burden resulting from the receipt of loan repayments. For FY 2004, the AIDS-LRP plans to award fifteen (15) contracts to individuals entering into initial two-year contracts, and five (5) contracts to individuals entering into one-year renewal contracts at a cost of $1.55 million.

Future Research Directions

In FY 2005, the OAR request includes $1.55 million for the AIDS LRP. The funding will be used to award contracts to twenty (20) health professionals conducting AIDS research.

Roadmap

To accelerate the pace of scientific discovery and hasten the translation of discoveries into new health care interventions, NIH has launched a historic set of initiatives known collectively as the NIH Roadmap for Medical Research. Soon after becoming NIH Director, Dr. Elias Zerhouni convened a series of meetings to chart a "roadmap" for medical research in the 21st century — a process that identified major opportunities and gaps in the biomedical research agenda that no single institute at NIH could tackle alone, but that are the responsibility of the agency as a whole. Developed with input from more than 300 nationally recognized leaders in academia, industry, government and the public, the NIH Roadmap provides a framework of the strategic investments that NIH needs to make to optimize its research portfolio. The NIH Roadmap strategy features 27 initiatives to be carried out by nine implementation groups arranged under three main themes: new pathways to discovery, research teams of the future, and re-engineering the clinical research enterprise.

Under New Pathways to Discovery, the NIH Roadmap aims to quantify and catalog some of the complex biological systems and seeks to build a better "toolbox" for today's biomedical researchers. Just as systemic treatises on anatomy and the perfection of the microscope in the 19th Century were key to modern medicine in the 20th Century, comprehensive databases of quantitative information on biochemical pathways and molecular interactions and tools to capture and manage that information will be pivotal to advances in 21st Century heath care. A few of the initiatives in this area are:

- Scientists at *National Technology Centers for Networks and Pathways* will conduct research to better understand the pathways and networks that enable communication among genes, molecules, and cells.

- *National Centers for Biomedical Computing* will generate and provide software and data management tools to enable researchers to share data gathered from large experiments allowing the best minds to work together more efficiently to tackle unsolved mysteries

Because the complexity of today's biomedical research increasingly requires scientists to move beyond the confines of their own disciplines, under the theme, Research Teams of the Future, the NIH Roadmap will encourage scientists and scientific institutions to test alternative models for conducting research. Examples of initiatives in this arena include:

- A major initiative under this theme is for *Exploratory Centers for Interdisciplinary Research*. The centers are expected to help scientists overcome the often substantial barriers to establishing interdisciplinary research efforts

- A NRSA program, *Interdisciplinary Health Research Training: Behavior, Environment, and Biology,* which is intended to help ensure the development of a cadre of scientists with the requisite skills and knowledge to integrate multiple scientific approaches and to work in interdisciplinary research teams to solve these complex health problems.

- A new type of research award, the NIH Director's Pioneer Award, has been designed to identify and fund investigators of exceptionally creative abilities, for a five-year period to allow them to develop and test novel conceptual and technological breakthroughs.

The third NIH Roadmap theme is Re-engineering Clinical Research. Although biomedical research has resulted in new prevention strategies and treatments for many diseases, future efforts to translate scientific discoveries into health care interventions require new partnerships, systems, and policies. A few of the initiatives in this area are:

- *National Electronic Clinical Trials and Research Network (NECTAR)* - This initiative aims to create an informatics infrastructure that will allow: more efficient business practices and processes, enhanced data sharing and analysis, coordinated oversight and improved patient protections, and rapid translation of research into clinical findings and practice.

- *Clinical Research Policy Coordination Initiative* - The multiple requirements of diverse regulatory and funding agencies may be an impediment to efficient clinical research. NIH is creating a focal point for working within the Federal system of clinical research oversight to promote the coordination of policies, requirements, and procedures concerning clinical research and, where appropriate, to help bring about streamlined approaches.

Taken together, the components of the NIH Roadmap are an ambitious vision for a more efficient and productive system of medical research, with the goal of improving the length and quality of human life. Moreover, the development and implementation of the NIH Roadmap represents a new approach to portfolio management. Building on earlier experience with trans-NIH endeavors, the NIH Roadmap planning process sets a new standard for responding to emerging needs and opportunities that do not fit clearly within the mission of a single or a small group of Institutes and Centers. The OD Roadmap request for FY 2005 is $60 million.

The Director's Discretionary Fund

In FY 2005 the NIH Director will continue to maintain a Director's Discretionary Fund (DDF) to allow the Director to respond quickly to new and emerging high priority research opportunities and health priorities. The DDF request for FY 2005 is $10 million. Also included in the DDF request is $60 million for Roadmap activities.

Other Areas of Interest

As part of the OD Operations, several OD offices such as the OER, the Office of Intramural Resarch (OIR), the OSP, and the Office of Management (OM) provide advice to the NIH Director, policy direction to the NIH research community, and administer centralized support services essential to the daily operation of the NIH. The budget request for these operational offices for
FY 2005 is $107.158 million. Within the OSP, the Office of Biotechnology Activities (OBA)

(OBA) coordinates the functions of the Recombinant DNA Advisory Committee (RAC); the Secretary's Committee on Genetic Testing (SACGT); and the Secretary's Advisory Committee on Xenotransplantation (SACX).